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10/734,631	12/11/2003	Mark A. Gallop	XENO-007/02US	2008

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EXAMINER	
RAMACHANDRAN, UMAMAHESWARI	
ART UNIT	**PAPER NUMBER**
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/734,631	GALLOP, MARK A.	
	Examiner	Art Unit	
	Umamaheswari Ramachandran	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 39-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 39-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/25/2004;4/4/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Restriction/Election

Applicant's election of group III claims 39-53 in the reply filed on 4/9/2007 is acknowledged. The restriction election has been made with traverse. The Applicants' argument to examine Group I along with elected Group III is found to be persuasive. Hence the claims of Group I, 1-17 will be rejoined and examined along with the claims 39-53 of Group III. The applicant has stated in the restriction/election remarks that a search of the subject matters of Group II in addition to the subject matter of Group III, would not be burdensome. Claims 18-38 of group II is drawn to an oral dosage of a fused GABA analog prodrug. The inventions of Groups I and III are related as methods and Group II as pharmaceutical composition. The inventions are distinct if the following can be shown: (1) that the method as claimed can be carried out with a different product or (2) that the product as claimed can be used for a different method. (See MPEP § 806.05(h). In the instant case the methods in the claims can use compounds with sulfhydryl moiety as protective agents in reducing the toxicity of various antineoplastic agents by administering an effective amount of the protective agent to a patient receiving one or more antineoplastic agents (U.S. 6,057,361). Groups II and III are distinct and independent for the above reasons and the examiner will be focusing on the methods of administration and methods of use to examine claims 1-17 and 39-53 and not on the composition for the searches. The inventions require different field of search (employ different search strategies) and the prior art applicable to the invention of the composition would not likely be applicable to the method of administration or method of

reducing toxicity. The search for all inventions would place an undue burden on the Office in view of the corresponding diversity in the field of search for each. All the claims directed to a method of administering GABA analogs are generic and hence the election of species requirement is withdrawn. The restriction requirement elected is made final. Claims 18-38 are withdrawn from consideration. Claims 1-17 and 39-53 are pending.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-17, 39-53 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-29 of U.S. Patent No. 6,833,140.

Claims 1-17, 39-53 of the instant application teach a method of orally administering a fused GABA analog and a method of reducing toxicity of an orally administered therapeutic fused GABA analog comprising making a fused GABA analog prodrug having a cleavable promoiety covalently bound to the therapeutic fused GABA analog; placing the prodrug in a sustained release oral dosage form; introducing the dosage form into the intestinal lumen of a patient by having the patient swallow the

dosage form; releasing the prodrug gradually into the intestinal lumen of the patient over a period of hours; and cleaving the promoiety from the prodrug to provide a therapeutic concentration of the fused GABA analog in the plasma of the patient.

Claims 1-29 of U.S. Patent No. 6,833,140 teach a method of reducing toxicity of an orally administered therapeutic GABA analog, comprising: formulating the GABA analog as a prodrug comprised of the therapeutic GABA analog covalently bound to a cleavable promoiety; placing the prodrug in a sustained release oral dosage form; introducing the dosage form into the intestinal lumen of a patient by having the patient swallow the dosage form; releasing the prodrug gradually into the intestinal lumen of the patient over a period of hours; and cleaving the promoiety from the prodrug to provide a therapeutic concentration of the GABA analog in the plasma of the patient, wherein the dosage form releases from 0 to 20% of the prodrug in 0 to 2 hours, from 20 to 50% of the prodrug in 2 to 12 hours, from 50 to 85% of the prodrug in 3 to 20 hours and greater than 75% of the prodrug in 5 to 18 hours. The patent also teaches a method of orally administering a GABA analog prodrug.

Claims 1-17 of the instant application are generic compared to claims 1-16 of the conflicting patent (U.S. 6,833,140). Claims 1-16 of the patent fall within the scope of the of the examined claims. Claims 1-16 of the patent anticipates claims 1-17 of the instant application.

Claims 39-53 of the instant application teach a method of administering a fused GABA analog and claims 18-29 of the patent (U.S. 6,833,140) teach a method of administering a GABA analog prodrug. Claim 18 of the patent is broad and

encompasses all GABA analog prodrugs including fused GABA analogs and the relationship between claims 39-53 of the instant application to claims 18-29 is species to genus claims. It would have been obvious to one of ordinary skill in the art to administer fused GABA analogs to patients as the patent teaches in general administration of all GABA analogs including fused GABA analogs.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent and the present application teach a method of administering GABA analogs.

Hence the claims 39-53 of the present application are an obvious variation of the patent.

Claims 1-17, 39-53 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17, 39-52 of copending Application No. 10/829,896 ('896).

Claims 1-17, 39-53 of the instant application teach a method of orally administering a fused GABA analog and a method of reducing toxicity of an orally administered therapeutic fused GABA analog comprising making a fused GABA analog prodrug having a cleavable promoiety covalently bound to the therapeutic fused GABA analog; placing the prodrug in a sustained release oral dosage form; introducing the dosage form into the intestinal lumen of a patient by having the patient swallow the dosage form; releasing the prodrug gradually into the intestinal lumen of the patient over a period of hours; and cleaving the promoiety from the prodrug to provide a therapeutic concentration of the fused GABA analog in the plasma of the patient.

Claims 1-17, 39-52 of the co-pending application '896 teach a method of orally administering a GABA analog prodrug and a method of reducing toxicity of an orally administered therapeutic GABA analog comprising formulating the GABA analog as a prodrug comprised of the therapeutic GABA analog covalently bound to a cleavable promoiety; placing the prodrug in a sustained release oral dosage form; introducing the oral dosage form into the intestinal lumen of the patient over period of hours; and cleaving the promoiety from the prodrug to provide a therapeutic concentration of the fused GABA analog in the plasma of the patient.

Claims 1-17, 39-53 of the instant application teaches a method of reducing toxicity of an orally administered fused GABA analog and a method of administering a fused GABA analog. Claims 18-29 of copending Application No. 10/829,896 teach a method of reducing toxicity of an orally administered GABA analog and a method of administering a GABA analog prodrug. Claims 1 and 39 of the copending Application ('896) is broad and encompasses all GABA analog prodrugs including fused GABA analogs and the relationship between claims 1-17, 39-53 of the instant application to claims 1-17, 39-52 is species to genus claims. It would have been obvious to one of ordinary skill in the art to administer fused GABA analogs to patients as the co-pending application ('896) teaches in general administration of all GABA analogs including fused GABA analogs.

Although the conflicting claims are not identical, they are not patentably

distinct from each other because the patent and the present application both teach a method of reducing toxicity administering GABA analog and a method of administration of GABA analog.

Hence the claims 1-17, 39-53 of the present application are an obvious variation of the co-pending application ('896).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-17, 39-53 are rejected under 35 U.S.C. 102(e) as being anticipated by Cundy et al (WO 02/100392).

Cundy teaches an oral dosage form of prodrugs of GABA analogs in a method of administering and reducing toxicity. The reference further teaches that the prodrugs of GABA analogs are metabolized to form an aldehyde. The reference teaches that the promoiety metabolizes to form pivalic acid that depletes carnitine in the patient and period of hours for the release of drug range from 6-12h. The reference also teaches the dosage form release ranging from 0-85% in 0-18 h. The reference teaches the area

under the curve is proportional to the dose of GABA analog administered and has a maximum plasma concentration. The reference also teach that Cmax concentrations being less than 60% or 75% than the Cmax obtained from administering an equivalent dose of the prodrug from an immediate release dosage form. The reference also teach the area under curve is substantially the same as the area under curve obtained by administering an equivalent dose of the prodrug from an immediate release oral dosage form. (see Abstract, p 60-66, claims 1-17, 39-52).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1 and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Gallop et al. (US 2003/0176398).

Gallop et al. teach a method of administering and reducing toxicity of an orally administered therapeutic GABA analogs that are typically labile in vivo (i.e., cleaved by either enzymatic or chemical means) to generate substantial quantities of a GABA analog before the prodrug is cleared from a patient and the promoiety derivative provided by cleavage and any metabolite thereof, is typically non-toxic when administered to a mammal (see Abstract, p2, para 0015, p36, para 0436, p35, para 0427, p34 para 0414, 0415). The reference teaches that the prodrug may be cleaved

prior to or after the absorption of the drug in the intestinal tract (para 0421), and the prodrugs can be delivered via sustained release systems, preferably oral sustained release systems (para 0415).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1-17, 39-53 are rejected under 35 U.S.C. 102(e) as being anticipated by Cundy et al. (U.S. 6,833,140).

Cundy et al. teach a method of reducing toxicity of an orally administered therapeutic GABA analog, comprising: formulating the GABA analog as a prodrug comprised of the therapeutic GABA analog covalently bound to a cleavable promoiety; placing the prodrug in a sustained release oral dosage form; introducing the dosage form into the intestinal lumen of a patient by having the patient swallow the dosage form; releasing the prodrug gradually into the intestinal lumen of the patient over a period of hours; and cleaving the promoiety from the prodrug to provide a therapeutic concentration of the GABA analog in the plasma of the patient. The reference further teaches that the prodrugs of GABA analogs are metabolized to form an aldehyde. The reference teaches that the promoiety metabolizes to form pivalic acid that depletes carnitine in the patient and period of hours for the release of drug range from 6-12h. The

reference also teaches the dosage form release ranging from 0-85% in 0-18 h. The reference teaches the area under the curve is proportional to the dose of GABA analog administered and has a maximum plasma concentration. The reference also teach that Cmax concentrations being less than 60% or 75% than the Cmax obtained from administering an equivalent dose of the prodrug from an immediate release dosage form. The reference also teach the area under curve is substantially the same as the area under curve obtained by administering an equivalent dose of the prodrug from an immediate release oral dosage form (See Abstract, col. 42, 43, claims 1-17, 39-52).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1 and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Gallop et al. (US 2004/0006132).

Gallop et al. teach a method of administering and reducing toxicity of an orally administered therapeutic GABA analogs that are typically labile in vivo (i.e., cleaved by either enzymatic or chemical means) to generate substantial quantities of a GABA analog before the prodrug is cleared from a patient and the promoiety derivative provided by cleavage and any metabolite thereof, is typically non-toxic when administered to a mammal (see Abstract, p2, para 0015, para 0038). The reference

teaches that the prodrug may be cleaved prior to or after the absorption of the drug in the intestinal tract (para 0441), and the prodrugs can be delivered via sustained release systems, preferably oral sustained release systems (para 0421).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1 and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Gallop et al. (US 2004/0077553).

Gallop et al. teach a method of administering and reducing toxicity of an orally administered therapeutic GABA analogs that are typically labile in vivo (i.e., cleaved by either enzymatic or chemical means) to generate substantial quantities of a GABA analog before the prodrug is cleared from a patient and the promoiety derivative provided by cleavage and any metabolite thereof, is typically non-toxic when administered to a mammal (see Abstract, p 51, claim 3, para 0015). The reference teaches that the prodrug may be cleaved prior to or after the absorption of the drug in the intestinal tract (para 0414), and the prodrugs can be delivered via sustained release systems, preferably oral sustained release systems (para 0409).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art

under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1 and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Gallop et al. (US 2003/0236200).

Gallop et al. teach a method of administering orally therapeutic prodrugs of GABA to a patient (see Abstract, p 51, claim 36). The reference teaches that a therapeutically effective dose of a GABA analog compound of the invention will provide therapeutic benefit with little or no toxicity (para 0298). The reference teaches that the prodrugs cleaved after the absorption of the drug in the intestinal tract may have the opportunity to be absorbed into the systemic circulation from the large intestine and are delivered by oral sustained release administration (para 0283).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1 and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by Gallop et al. (U.S. 2003/0171303).

Gallop et al. teach a method of administering orally therapeutic prodrugs of GABA to a patient (see Abstract). The reference teaches that fused GABA analog prodrug compounds may be cleaved either chemically and/or enzymatically in the intestinal lumen (para 0177, 0178). The reference teaches that a therapeutically effective dose of a GABA analog compound of the invention will provide therapeutic benefit with little or no toxicity (para 0193). The reference teaches that the prodrugs can be delivered by oral sustained release systems (para 0172).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1-17, 39-53 are rejected under 35 U.S.C. 102(e) as being anticipated by Gallop et al. (U.S. 2003/0083382).

Cundy et al. teach a method of reducing toxicity of an orally administered therapeutic GABA analog, comprising: formulating the GABA analog as a prodrug comprised of the therapeutic GABA analog covalently bound to a cleavable promoiety; placing the prodrug in a sustained release oral dosage form; introducing the dosage form into the intestinal lumen of a patient by having the patient swallow the dosage form; releasing the prodrug gradually into the intestinal lumen of the patient over a period of hours; and cleaving the promoiety from the prodrug to provide a therapeutic

concentration of the GABA analog in the plasma of the patient. The reference further teaches that the prodrugs of GABA analogs are metabolized to form an aldehyde. The reference teaches that the promoiety metabolizes to form pivalic acid that depletes carnitine in the patient and period of hours for the release of drug range from 6-12h. The reference also teaches the dosage form release ranging from 0-85% in 0-18 h. The reference teaches the area under the curve is proportional to the dose of GABA analog administered and has a maximum plasma concentration. The reference also teach that Cmax concentrations being less than 60% or 75% than the Cmax obtained from administering an equivalent dose of the prodrug from an immediate release dosage form. The reference also teach the area under curve is substantially the same as the area under curve obtained by administering an equivalent dose of the prodrug from an immediate release oral dosage form (See Abstract, p23-25, claims 1-17, 39-52).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Conclusion

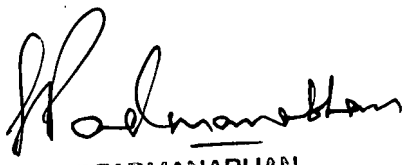
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone

number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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